

In the Specification

Please replace paragraph [0002] with the following:

Technical Field of the Invention

[0002] This ~~invention~~ disclosure relates a new composition containing halogenated compounds for (1) the treatment of viral, bacterial, parasitical, fungal infections, or infections generated from non-conventional transmissible agents; (2) the treatment of chronic, progressive or acute inflammation; (3) immuno-modulator treatments, and/or tissue healing stimulator treatments; and (4) pre- and/or per- and/or post-surgical irrigations. The ~~invention~~ composition is particularly helpful as a local use antiseptic.

Please replace paragraph [0068] with the following:

Summary of the Invention

[0068] This ~~invention~~ relates to I provide a pharmaceutical composition including at least one halogenated compound, and at least one N-halogenated derivative of at least one compound selected from zwitterionic and/or amino acid compounds, where the composition does not generate substantial stimulation of myeloperoxidase activity in a mammal.

Please replace paragraph [0069] with the following:

[0069] This ~~invention~~ I also relates to provide a method of preparing a pharmaceutical composition including mixing at least one halogenated compound and at least one zwitterionic compound and/or at least one amino acid or their derivatives, and optionally at least one excipient to obtain at least one N-halogenated derivative, and at least one halogenated compound in a sufficient therapeutic amount to not substantially stimulate myeloperoxidase activity in a mammal.

Please replace paragraph [0070] with the following:

[0070] ~~This invention~~ I further relates to provide a method for treatment and/or preventing viral infections, and/or bacterial infections, and/or parasitical infections and/or fungal infections and/or diseases generated from non-conventional transmissible agents, in humans or animals including administering to a human or animal a pharmaceutically effective amount of a pharmaceutical composition including at least one halogenated compound, and at least one N-halogenated derivative of at least one compound selected from zwitterionic compounds and/or the amino acids or their derivatives without substantial stimulation or myeloperoxidase activity in the human or animal.

Please replace paragraph [0072] with the following:

[0072] Consequently, ~~this invention provides~~ I provide a pharmaceutical composition comprising (i) at least one halogenated compound and (ii) at least one N-halogenated derivative of at least one compound selected from zwitterionic and/or amino acid compounds.

Please replace paragraph [0073] with the following:

[0073] Within those compositions ~~according to the invention~~, the halogenated compound (i) is an antiseptic.

Please replace paragraph [0074] with the following:

[0074] Amino acids included in the constitution of compositions ~~according to the invention~~ can be natural amino acids, derivatives or analogous of the latter.

Please replace paragraph [0075] with the following:

[0075] More particularly, the halogen of the (i) halogenated compounds and the (ii) N-halogenated derivatives of the ~~invention~~ composition, similar or different, may be fluorine, iodine, bromine, and mainly chlorine.

Please replace paragraph [0077] with the following:

[0077] The ~~invention~~ composition is remarkable from its robust properties such as large spectrum of application such as anti-inflammatory, immunity modulation, and tissue healing stimulation as well as those without stimulation of myeloperoxidase activity.

Please replace paragraph [0078] with the following:

[0078] The hypochlorite titer of the ~~invention~~ composition is preferably below or equal to about 1 mole/liter of available chlorine, and can be adapted to clinical use. Usefully, the ~~invention~~ composition contains a hypochlorite of alkaline metal. Preferably, the ~~invention~~ composition contains a sodium hypochlorite *q.s.* with a minimum titer of available chlorine that is greater than or equal to about 1 picomole/liter.

Please replace paragraph [0079] with the following:

[0079] The N-chloramine titer of the ~~invention~~ composition is preferably less than or equal to about 5 moles/liter, and may be adapted to clinical use. Usefully, the ~~invention~~ composition contains an N-halogenated derivative, such as the taurine N-chloramine, with a concentration between about 5 moles/liter and about 0.01 femtomoles/liter. Preferably, the ~~invention~~ composition contains a N-halogenated derivative such as the taurine N-chloramine, *q.s.* with a minimum titer greater than or equal to about 0.01 femtomoles/liter.

Please replace paragraph [0080] with the following:

[0080] The (i) halogenated compound and the (ii) N-halogenated derivative are associated in the composition ~~according to the invention~~ with an excipient, such as purified water, in accordance with therapeutic use. Preferably, it concerns an osmotic (isotonic) purified water. This excipient may contain diverse agents, pharmaceutically compatible with both (i) the halogenated compound and (ii) the N-halogenated derivative, and which can allow for modification of some physicochemical

properties such as stability, pH, pKa, density, solubility, viscosity, coloring, water/ectanol sharing factor, and surface-active, oxidative, olfactory, or gustatory properties of the ~~invention~~ composition *via* a suitable agent addition. The ~~invention~~ composition may also contain some anti-oxidants and/or amino acids that have a dilution effect *via* neutralization of some alkaline metal hypochlorite molecules. These anti-oxidants, amino acids and their N-halogenated derivatives should have a neutral pharmacological activity or its activity should be pointed to therapeutic aims and should not exercise a direct stimulation of myeloperoxidase activity in the presence of ~~invention~~ composition active agents.

Please replace paragraph [0081] with the following:

[0081] ~~The invention~~ I also ~~concerns~~ provide for the preparation of the composition described above.

Thus, this composition can be sold in a form to prepare before use, *i.e.*, (i) the halogenated compound(s) can be mixed with (ii) the N-halogenated derivative(s) and one or several excipients. This presentation form can be considered if it is required to guarantee the best time stability of the composition and, in particular, the active agents that constitute the latter. However, even in a presentation where the constituting products would be associated, the ~~invention~~ composition can be sold with an excipient, such as purified water according to the therapeutic use. Preferably, this should be an osmotic (isotonic) purified water. In addition, this excipient may contain diverse agents pharmaceutically compatible with the totality of final composition molecules, which allow for the modification of some physicochemical properties of the ~~invention~~ composition *via* an addition of suitable agent(s) such as stability, pH, pKa, density, solubility, viscosity, coloring, water/ectanol sharing factor, and surface-active, oxidative, olfactory, or gustatory properties.

Please replace paragraph [0082] with the following:

[0082] The ~~invention~~ composition can also be prepared before its administering to the patient *via* a mixture comprising:

- (i) at least one halogenated compound, and
- (ii) at least one N-halogenated derivative of at least one compound selected from zwitterionic and/or amino acid compounds, and their derivatives.

Please replace paragraph [0087] with the following:

[0087] Favorably, the ~~invention~~ composition may be prepared *via* a mixture of the two solutions described above with at least one excipient according to therapeutic use such as purified water. It preferably contains the osmotic (isotonic) purified water. In addition, this excipient can contain diverse agents, pharmaceutically compatible with all molecules of the final mixing to modify some physicochemical properties of the ~~invention~~ composition such as stability, pH, pKa, density, solubility, viscosity, coloring, water/ectanol sharing factor, and surface-active, oxidative, olfactory, or gustatory properties *via* an addition of suitable agent(s).

Please replace paragraph [0088] with the following:

[0088] In addition to the process described above, the ~~invention~~ composition may be prepared *via* a mixture of the two following solutions:

- (i) at least one halogenated compound as defined above, which is usefully displayed in a liquid or a semi-liquid (such as a gel) solution form, preferably within an excipient as described above,
- (iii) at least one zwitterionic compound and/or at least one amino acid and/or at least one primary or secondary amine, (the zwitterionic compound and/or amino acid and/or primary or

secondary amino amine are later referred to as “Zw/Aam”), which is usefully displayed in a liquid or a semi-liquid (such as a gel) solution form, favorably within an excipient as described above, to obtain an association of both (i) at least one halogenated compound and (ii) at least one N-halogenated derivative, and this with a sufficient therapeutic amount of molecules to inhibit myeloperoxidase activity.

Please replace paragraph [0092] with the following:

[0092] The hypochlorite titer of the first active solution (i) should take into consideration the stoichiometry and reactivity level of the reaction between hypochlorous acid and Zw/Aam molecules. In case this reaction is not complete, remaining Zw/Aam molecules should not stimulate myeloperoxidase activity in the presence of ~~invention~~ composition active agents.

Please replace paragraph [0093] with the following:

[0093] In case the stoichiometry is 1/1 and with a complete reaction (*e.g.*, between hypochlorous acid and taurine), the hypochlorite titer of the first active solution is preferably lower than or equal to about 6 moles/liter of available chlorine, and must be adapted both to the Zw/Aam molecule amount of the second solution and to clinical status. In this preparation method, the halide solution (i) favorably contains an alkaline metal hypochlorite. Even more preferably, the haloid solution (i) contains sodium hypochlorite *q.s.* with an available chlorine titer between about 6 moles/liter and about 1,000.01 femtomoles/liter. The taurine titer of the second solution (iii) of this ~~invention~~ preparation method is preferably lower than or equal to about 1 moles/liter and may be adapted to clinical use. It is useful for the second solution (iii) of this invention preparation method to have a taurine concentration between about 5 moles/liter and about 0.01 femtomole/liter. Even more preferably, the second solution (iii) of this preparation method has a taurine titer greater than or equal to about 0.01 femtomole/liter.

Please replace paragraph [0094] with the following:

[0094] The excipient(s) preferably added in methods described above may be used as a secondary diluting solution with the aim to adapt the treatment to the clinical status. It usefully concerns osmotic (isotonic) purified water. This excipient will favorably be similar to the excipient used for the compounds and derivatives that have been mixed, and if they are not identical, the excipient should be pharmaceutically compatible to be mixed with the other excipient(s), before all clinical uses. In addition, this excipient can contain diverse agents, pharmaceutically compatible with all molecules of the final therapeutic mixture with the object of modifying some physicochemical properties of the ~~invention~~ composition such as stability, pH, pKa, density, solubility, viscosity, coloring, water/ectanol sharing factor, and surface-active, oxidative, olfactory, or gustatory properties *via* an addition of a suitable agent(s).

Please replace paragraph [0096] with the following:

[0096] The composition ~~according to the invention~~ can also be sold in a form adapted to local use, *e.g.*, a gel or an aerosol.

Please replace paragraph [0097] with the following:

[0097] The above-mentioned ~~invention~~ composition is particularly useful in humans or animals for treatments of viral infections and/or bacterial infections and/or parasitical infections and/or fungal infections and/or diseases generated from non-conventional transmissible agents; and/or for treatments of chronic, progressive or acute inflammation; and/or for immunity modulator treatments; and/or for tissue regeneration stimulator treatments. In addition, the therapeutic composition may be used in *pre*-surgical irrigations and/or *per*-surgical irrigations and/or *post*-surgical irrigations.

Please replace paragraph [0098] with the following:

[0098] ~~The invention concerns~~ I particularly provide for the local treatment of infections due to herpesviridae family virus.

Please replace paragraph [0099] with the following:

[0099] The ~~invention~~ composition is preferably used locally aiming to remove secondary effects, e.g., atherosclerosis. It can be applied to all external or internal mucous (e.g., oral, genital, vaginal, ophthalmic, otic, sinus, nose-and-throat, dermal, and the like). The ~~invention~~ composition may appear under an adapted form for this administration, such as in a semi-liquid form (e.g., a gel) via an addition of one or several compatible pharmaceutical substances e.g., cellulose, amino acids, peptides, and/or proteins.

Please replace paragraph [0100] with the following:

[0100] The ~~invention~~ composition may also be adapted to clinical status and/or injured mucous. This adaptation is executed via a concentration change of active products of the therapeutic solutions.

Please replace paragraph [0112] with the following:

[0112] The composition ~~according to the invention~~ is useful for local treatment of diseases or inflammatory processes that can be chronic, and/or progressive and/or acute. The composition is also recommended for ~~pre-surgical~~ pre-surgical irrigation and/or per-surgical irrigation and/or post-surgical irrigation of internal and/or external mucous and of opened-injuries. The ~~invention~~ method more particularly concerns a treatment method of lesions and infections described above, which comprises contacting the ~~invention~~ composition on mucous that must be treated, (for non-restricting example) between 2 and 3 times a day and approximately during 20 to 60 seconds, not followed by a rinsing. The composition amount employed should be sufficient to not generate a total neutralization

of the therapeutic active agents. In the therapeutic use, the ~~invention~~ solution should not stay static. Concentrations of the composition ~~invention~~ should be adapted to the evolution of the clinical status until healing.

Please replace paragraph [0113] with the following:

[0113] ~~The invention~~ I more particularly ~~concerns~~ provide for the local treatment of lesions and infections linked to chronic and/or acute ~~parodontitis~~ periodontitis. Thus, the ~~invention~~ composition is usefully adapted for irrigation of periodontal pockets, with the aim for removing these periodontal pockets as the composition has both antiseptic and anti-inflammatory activities, and acts as an immunity modulator and healing stimulator of periodontal tissues (i.e., alveolar bone, alveolodental ligament and gingiva).

Please replace paragraph [0130] with the following:

[0130] In addition, ~~the invention~~ I also ~~concerns~~ provide for bone-filling surgical periodontal treatments with some biomaterials associated with the ~~invention~~ composition and/or one of its components.